EXPRESS MAIL NO.: EV 811 558 485 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

U.S. Patent No.: 7,122,544 B2 (U.S. application no. 10/004,642, filed December 4, 2001)

Issued: October 17, 2006

Inventor(s): Kois et al.

For: ANILINOPYRIMIDINE DERIVATIVES AS IKK INHIBITORS AND COMPOSITIONS AND METHODS RELATED THERETO

Attorney Docket No.: 10624-049-999
(CAM: 700755-999048)

REQUEST FOR CERTIFICATE OF CORRECTION
UNDER 37 C.F.R. §1.322

Attention Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Patentee hereby respectfully requests the issuance of a Certificate of Correction in connection with the above-identified patent. The correction is listed on the attached Form PTO-1050.

The error was made by the United States Patent and Trademark Office ("USPTO") in connection with the above patent, wherein at:

Claim 1, column 300, line 25, please replace "napbthyl" with -- naphthyl --;

Claim 1, column 301, line 8, please replace "beazimidazolyly" with -- benzimidazolyl --;

Claim 1, column 301, line 9, please replace "beazothiazolyl" with -- benzothiazolyl --;

Claim 8, column 302, line 26, please replace "sulfmylakyl" with -- sulfinylalkyl --;

Claim 8, column 302, line 65, please replace "pyrazuiyl" with -- pyrazinyl --;

Claim 8, column 303, line 14, please replace "plithalazinyl" with -- phthalazinyl --;

Claim 8, column 3043, line 16, please replace "piperazmyl" with -- piperazinyl --;

Claim 9, column 303, line 42, please replace "nanhthyl" with -- naphthyl --;

Claim 9, column 304, line 39, please replace "terrhydrofuranyl" with -- tetrahydrofuranyl --; and

Claim 14, column 305, line 40, please replace "ossteoarthm-itis" with -- osteoarthritis --.

Enclosed is a copy of a Reply to Non-Final Office Action Under 37 C.F.R. § 1.111 filed in the USPTO in connection with the above-identified patent application on February 15, 2005 (the "Response") evidencing the corrections as set forth above. The enclosed copy of the Response is date-stamped "FEB 15 2005" evidencing its receipt by the UPSTO.

No fee is believed to be due in connection with this request since the errors were made by the USPTO. Should any fees be required, however, please charge such fees to Jones Day Deposit Account No. 50-3013. Please issue a certificate of correction as soon as possible.

Respectfully submitted,

Anthony M. Insogna, Reg. No. 35,203

By: Michael J. Bruner, Reg. No. 47,458

Date: November 17, 2006

By: Michael J. Bruner (Reg. No. 47,458)
JONES DAY
222 East 41st Street
New York, New York 10017
(212) 326-3939

For: Anthony M. Insogna (Reg. No. 35,203)
JONES DAY
12750 High Bluff Drive, Suite 300
San Diego, California 92130
(858) 314-1130

PRINTER'S TRIM LINE

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7,122,544 B2

DATED : October 17, 2006

INVENTOR(S) : Kois et al.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

At Claim 1, column 300, line 25, please replace "napbthyl" with -- naphthyl --;
At Claim 1, column 301, line 8, please replace "beazimidazolyly" with -- benzimidazolyl --;
At Claim 1, column 301, line 9, please replace "beazothiazolyl" with -- benzothiazolyl --;
At Claim 8, column 302, line 26, please replace "sulfmylakyl" with -- sulfinylalkyl --;
At Claim 8, column 302, line 65, please replace "pyrazuiyl" with -- pyrazinyl --;
At Claim 8, column 303, line 14, please replace "plithalazinyl" with -- phthalazinyl --;
At Claim 8, column 3043, line 16, please replace "piperazmyl" with -- piperazinyl --;
At Claim 9, column 303, line 42, please replace "nanhthyl" with -- naphthyl --;
At Claim 9, column 304, line 39, please replace "terrhydrofuranyl" with -- tetrahydrofuranyl --; and
At Claim 14, column 305, line 40, please replace "ossteoarthm-itis" with -- osteoarthritis --.

MAILING ADDRESS OF SENDER:
JONES DAY
222 East 41st Street
New York, New York 10017
(858) 314-1130
ATI-2249536v1
FORM PTO 1050

PATENT NO. 7,122,544 B2

No. of add'l. copies

NOV 22 2006 30¢ perpage

=>

Express Mail No.: EV 452 774 46 6US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Kois et al.

Confirmation No.: 6698

Application No.: 10/004,642

Group Art Unit: 1624

Filed: December 4, 2001

Examiner: Raymond, Richard L.

For: ANILINOPYRIMIDINE DERIVATIVES AS IKK INHIBITORS AND COMPOSITIONS AND METHODS RELATED THERETO

Attorney Docket No.: 10624-049-999

(CAM: 700755-999048)

REPLY TO NON-FINAL OFFICE ACTION UNDER 37 C.F.R. § 1.111

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

In response to the Non-final Office Action mailed August 17, 2004 in connection with the above-identified application, please enter the following amendments and consider the following remarks intended to place this application into form for allowance.

Submitted herewith is: (i) a supplemental Form PTO-1449 listing reference DD; (ii) a copy of a Form PTO-1449 form with literature reference CG (with publication date provided) initialed by Examiner Ford; and (iii) a Petition for Extension of Time Under 37 C.F.R. § 1.136(a) for three (3) months with provision for the required fee (in duplicate).

Amendments to the claims are reflected in the listing of claims which begins on page 2 of this paper.

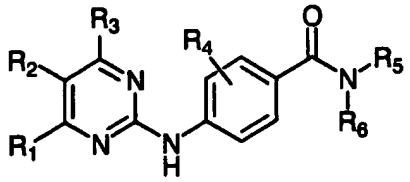
Remarks begin on page 13 of this paper.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims

1. (Currently Amended) A compound having the structure:



(I)

or a pharmaceutically acceptable salt thereof,

wherein:

R_1 is phenyl, naphthyl, ~~napthyly, pyridyl, furyl,~~ benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, ~~isoxazolyl, pyrazolyl,~~ isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, or quinazolinyl, optionally substituted with one to four substituents independently selected from R_7;

R_2 is hydrogen;

R_3 is hydrogen or lower alkyl;

R_4 represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl and lower alkoxy;

R_5 and R_6 are the same or different and independently $-R_8$, $-(CH_2)_aC(=O)R_9$,

$-(CH_2)_aC(=O)OR_9$, $-(CH_2)_aC(=O)NR_9R_{10}$, $-(CH_2)_aC(=O)NR_9(CH_2)_bC(=O)R_{10}$,

$-(CH_2)_aNR_9C(=O)R_{10}$, $-(CH_2)_aNR_{11}C(=O)NR_9R_{10}$, ~~$-(CH_2)_aNR_9R_{10}$~~, $-(CH_2)_aOR_9$,

$-(CH_2)_aSO_cR_9$, or $-(CH_2)_aSO_2NR_9R_{10}$;

or R_5 and R_6 taken together with the nitrogen atom to which they are attached to form a substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl;

R_7 is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylakyl, sulfonylalkyl, hydroxyalkyl, phenyl or naphthyl, substituted phenyl or naphthyl, aralkyl, substituted aralkyl, substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl, heterocyclealkyl, substituted heterocyclealkyl, $-C(=O)OR_8$, $-OC(=O)R_8$, $-C(=O)NR_8R_9$, $-C(=O)NR_8OR_9$, $-SO_cR_8$, $-SO_cNR_8R_9$, $-NR_8SO_cR_9$, $-NR_8R_9$, $-NR_8C(=O)R_9$, $-NR_8C(=O)(CH_2)_bOR_9$, $-NR_8C(=O)(CH_2)_bR_9$, $-O(CH_2)_bNR_8R_9$, or substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl fused to phenyl;

R_8, R_9, R_{10}, and R_{11} are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, phenyl or naphthyl, substituted phenyl or naphthyl, aralkyl, substituted arylalkyl, substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl,

benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl, heterocyclealkyl or substituted heterocyclealkyl;

or R_8 and R_9 taken together with the atom or atoms to which they are attached to form a substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl;

a and *b* are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2.

2. (Previously Presented) The compound of claim 1 wherein R_5 and R_6, taken together with the nitrogen atom to which they are attached, form a substituted or unsubstituted morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydropirimidinyl, tetrahydrothiophenyl, tetrahydrothiopyranyl, tetrahydropyrimidinyl, tetrahydrothiophenyl or tetrahydrothiopyranyl.

3-6. (Canceled)

7. (Previously Presented) The compound of claim 1 wherein R_1 is phenyl or naphthyl.

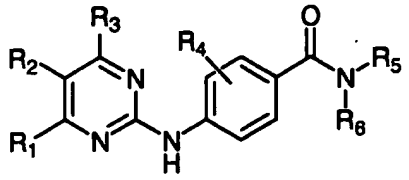
8. (Previously Presented) The compound of claim 3 wherein R_5 and R_6, taken together with the nitrogen atom to which they are attached, form piperazinyl.

9. (Previously Presented) The compound of claim 3 wherein R_5 and R_6, taken together with the nitrogen atom to which they are attached, form piperidinyl.

10. (Previously Presented) The compound of claim 3 wherein R_5 and R_6, taken together with the nitrogen atom to which they are attached, form morpholinyl.

11. (Previously Presented) A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier.

12. (Currently Amended) A method for treating a condition responsive to IKK-2 inhibition, comprising administering to a patient in need thereof and effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

R_1 is phenyl, naphthyl, ~~napthyly, pyridyl, furyl,~~ benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, ~~isoxazolyl, pyrazolyl,~~ isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, or quinazolinyl, optionally substituted with one to four substituents independently selected from R_7;

R_2 and R_3 are the same or different and are independently hydrogen or lower alkyl;

R_4 represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R_5 and R_6 are the same or different and independently $-R_8$, $-(CH_2)_aC(=O)R_9$,

$-(CH_2)_aC(=O)OR_9$, $-(CH_2)_aC(=O)NR_9R_{10}$, $-(CH_2)_aC(=O)NR_9(CH_2)_bC(=O)R_{10}$,

$-(CH_2)_aNR_9C(=O)R_{10}$, $-(CH_2)_aNR_{11}C(=O)NR_9R_{10}$, ~~$-(CH_2)_aNR_9R_{10}$~~, $-(CH_2)_aOR_9$,

$-(CH_2)_aSO_cR_9$, or $-(CH_2)_aSO_2NR_9R_{10}$;

or R_5 and R_6 taken together with the nitrogen atom to which they are attached to form a substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl;

R_7 is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylakyl, sulfonylalkyl, hydroxyalkyl, phenyl or naphthyl, substituted phenyl or naphthyl, aralkyl, substituted aralkyl, substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl,

heterocyclealkyl, substituted heterocyclealkyl, $-C(=O)OR_8$, $-OC(=O)R_8$, $-C(=O)NR_8R_9$, $-C(=O)NR_8OR_9$, $-SO_cR_8$, $-SO_cNR_8R_9$, $-NR_8SO_cR_9$, $-NR_8R_9$, $-NR_8C(=O)R_9$, $-NR_8C(=O)(CH_2)_bOR_9$, $-NR_8C(=O)(CH_2)_bR_9$, $-O(CH_2)_bNR_8R_9$, or substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl fused to phenyl;

R_8, R_9, R_{10} and R_{11} are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, phenyl or naphthyl, substituted phenyl or

naphthyl, aralkyl, substituted arylalkyl, substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl, heterocyclealkyl or substituted heterocyclealkyl;

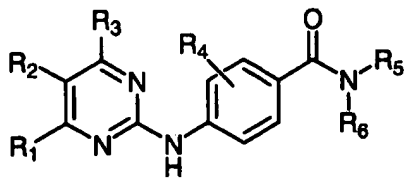
or R_8 and R_9 taken together with the atom or atoms to which they are attached to form a substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl;

a and *b* are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2,

wherein the condition is an inflammatory condition, an autoimmune condition, a cardiovascular condition, a metabolic condition, an ischemic condition, an infectious disease, stroke, epilepsy, Alzheimer's disease, Parkinson's disease or cancer.

13. (Currently Amended) A method for treating an inflammatory condition comprising administering to a patient in need thereof and effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

R_1 is phenyl, naphthyl, ~~naphthyl, pyridyl, furyl,~~ benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, ~~isoxazolyl, pyrazolyl,~~ isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, or quinazolinyl optionally substituted with one to four substituents independently selected from R_7;

R_2 and R_3 are the same or different and are independently hydrogen or lower alkyl;

R_4 represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R_5 and R_6 are the same or different and independently $-R_8$, $-(CH_2)_aC(=O)R_9$, $-(CH_2)_aC(=O)OR_9$, $-(CH_2)_aC(=O)NR_9R_{10}$, $-(CH_2)_aC(=O)NR_9(CH_2)_bC(=O)R_{10}$, $-(CH_2)_aNR_9C(=O)R_{10}$, $-(CH_2)_aNR_{11}C(=O)NR_9R_{10}$, ~~$-(CH_2)_aNR_9R_{10}$~~, $-(CH_2)_aOR_9$, $-(CH_2)_aSO_cR_9$, or $-(CH_2)_aSO_2NR_9R_{10}$;

or R_5 and R_6 taken together with the nitrogen atom to which they are attached to form a substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl;

R_7 is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylakyl, sulfonylalkyl, hydroxyalkyl, phenyl or naphthyl, substituted phenyl or naphthyl, aralkyl, substituted aralkyl, substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl,

hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl, heterocyclealkyl, substituted heterocyclealkyl, $-C(=O)OR_8$, $-OC(=O)R_8$, $-C(=O)NR_8R_9$, $-C(=O)NR_8OR_9$, $-SO_cR_8$, $-SO_cNR_8R_9$, $-NR_8SO_cR_9$, $-NR_8R_9$, $-NR_8C(=O)R_9$, $-NR_8C(=O)(CH_2)_bOR_9$, $-NR_8C(=O)(CH_2)_bR_9$,

$-O(CH_2)_bNR_8R_9$, or substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl fused to phenyl;

R_8, R_9, R_{10} and R_{11} are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, phenyl or naphthyl, substituted phenyl or naphthyl, aralkyl, substituted arylalkyl, substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl, heterocyclealkyl or substituted heterocyclealkyl;

or R_8 and R_9 taken together with the atom or atoms to which they are attached to form a substituted or unsubstituted pyridyl, furyl, benzofuranyl, thiophenyl, benzothiophenyl, quinolinyl, pyrrolyl, indolyl, oxazolyl, benzoxazolyl, imidazolyl, benzimidazolyl, thiazolyl, benzothiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, cinnolinyl, phthalazinyl, quinazolinyl, morpholinyl, pyrrolidinonyl, pyrrolidinyl, piperidinyl, piperazinyl, hydantoinyl, valerolactamyl, oxiranyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyrindinyl, tetrahydrothiophenyl, tetrahydropyrimidinyl, or tetrahydrothiopyranyl;

NOV 2 2 2006

a and *b* are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2.

14. (Previously Presented) The method of claim 13 wherein the inflammatory condition is rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gout, asthma, bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, cystic fibrosis, inflammatory bowel disease, irritable bowel syndrome, mucous colitis, ulcerative colitis, Crohn's disease, gastritis, esophagitis, hepatitis, pancreatitis, nephritis, psoriasis, eczema, dermatitis, multiple sclerosis, Lou Gehrig's disease, sepsis, conjunctivitis, acute respiratory distress syndrome, purpura, nasal polip or lupus erythematosus.

15-23. (Canceled)

24. (Previously Presented) A method for treating an inflammatory condition comprising administering to a patient in need thereof an effective amount of a compound or pharmaceutically acceptable salt of the compound of claim 1.

25. (Previously Presented) The method of claim 24 further comprising administering an effective amount of an anti-inflammatory agent.

26. (Previously Presented) The method of claim 25, wherein the anti-inflammatory agent is salicylic acid, acetylsalicylic acid, methyl salicylate, diflunisal, salsalate, olsalazine, sulfasalazine, acetaminophen, indomethacin, sulindac, etodolac, mefenamic acid, meclofenamate sodium, tolmetin, ketorolac, dichlofenac, ibuprofen, naproxen, naproxen sodium, fenoprofen, ketoprofen, flurbinprofen, oxaprozin, piroxicam, meloxicam, ampiroxicam, droxicam, pivoxicam, tenoxicam, nabumetome, phenylbutazone, oxyphenbutazone, antipyrine, aminopyrine, apazone and nimesulide, zileuton, aurothioglucose, gold sodium thiomalate, auranofin, colchicine, allopurinol, probenecid, sulfinpyrazone, benzbromarone, enbrel, infliximab, anarkinra, celecoxib or rofecoxib.

27. (Previously Presented) The method of claim 24, wherein the inflammatory condition is rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gout, asthma, bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, cystic fibrosis, inflammatory bowel disease, irritable bowel syndrome, mucous colitis, ulcerative colitis,

Crohn's disease, gastritis, esophagitis, hepatitis, pancreatitis, nephritis, psoriasis, eczema, dermatitis, multiple sclerosis, Lou Gehrig's disease, sepsis, conjunctivitis, acute respiratory distress syndrome, purpura, nasal polip or lupus erythematosus.

28-37. (Canceled)

38. (Canceled) The compound of claim 7 wherein aryl is phenyl.

39. (Previously Presented) The method of claim 12 wherein the cardiovascular or metabolic condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart, kidney, liver, and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure.

40. (Previously Presented) The method of claim 12 wherein the infectious disease is a viral infection.

41. (Previously Presented) The method of claim 40 wherein the viral infection is caused by human immunodeficiency virus, hepatitis B virus, hepatitis C virus, human papilomavirus, human T-cell leukemia virus or Epstein-Barr virus.

42. (Previously Presented) The method of claim 12 wherein the cancer is of the colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, testes, urinary bladder, ovary or uterus.

43 (Previously Presented) The method of claim 42 further comprising administering an effective amount of an anti-cancer agent or radiation therapy.

44. (Previously Presented) The method of claim 43 wherein the anti-cancer agent is cyclophosphamide, Ifosfamide, trofosfamide, Chlorambucil, carmustine (BCNU), Lomustine (CCNU), busulfan, Treosulfan, Dacarbazine, Cisplatin, carboplatin, vincristine, Vinblastine, Vindesine, Vinorelbine, paclitaxel, Docetaxol, etoposide, Teniposide, Topotecan, 9-aminocamptothecin, camptoirinotecan, crisnatol, mytomycin C, methotrexate, Trimetrexate, mycophenolic acid, Tiazofurin, Ribavirin, EICAR, hydroxyurea, deferoxamine, 5-fluorouracil, Floxuridine, Doxifluridine, Ratitrexed, cytarabine (ara C), cytosine arabinoside, fludarabine, mercaptopurine, thioguanine, Tamoxifen, Raloxifene,

megestrol, goscrclin, Leuprolide acetate, flutamide, bicalutamide, B 1089, CB 1093, KH 1060, vertoporfin (BPD-MA), Phthalocyanine, photosensitizer Pc4, demethoxyhypocrellin A (2BA-2-DMHA), interferon-α, interferon-γ, tumor-necrosis factor, Lovastatin, 1-methyl-4-phenylpyridinium ion, staurosporine, Actinomycin D, Dactinomycin, bleomycin A2, Bleomycin B2, Peplomycin, daunorubicin, Doxorubicin (adriamycin), Idarubicin, Epirubicin, Pirarubicin, Zorubicin, Mitoxantrone, verapamil or thapsigargin.

REMARKS

Claims 1, 2, 7-14, 24-27 and 39-44 are presently pending. Claims 1, 12 and 13 have been amended to no longer recite that R_1 can be pyridyl, furyl, pyrazolyl or isoxazolyl. Claims 1, 12 and 13 have been further amended to no longer recite that R^5 or R^6 can be $-(CH_2)_aNR_9R_{10}$. Claims 1, 12 and 13 have also been amended to correct an inadvertent typographical error in connection with the spelling of the term "naphthyl." Claim 38 has been canceled without prejudice. No new matter has been added.

Applicant reserves the right to prosecute the subject matter of any canceled, withdrawn or amended claim or any other unclaimed subject matter in one or more continuation, divisional or continuation-in-part applications.

I. Provisional Rejection of Claims 12-14, 24-27 and 39-44 Under the Judicially Created Doctrine of Obviousness-Type Double Patenting

Claims 12-14, 24-27 and 39-44 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 17 and 27 of co-pending Application No. 10/004,645 (the "'645 application").

Applicant requests that the rejection of claims 12-14, 24-27 and 39-44 under obviousness-type double patenting be held in abeyance until such time as allowable subject matter of all pending claims is indicated.

Accordingly, Applicant respectfully requests that the provisional rejection of claims 12-14, 24-27 and 39-44 under the judicially created doctrine of obviousness-type double patenting be withdrawn.

II. Rejection of Claims 1, 7, 11 and 38 Under 35 U.S.C. § 102(b or e)

Claims 1, 7, 11 and 38 stand rejected under 35 U.S.C. § 102(b or e) as allegedly anticipated by U.S. Patent No. 6,693,108 to Green *et al.* ("Green"), U.S. Patent No. 6,114,333 to Davis *et al.*, ("Davis I"), U.S. Patent No. 6,552,029 to Davis *et al.* ("Davis II"), U.S. Patent No. 4,788,195 to Torley *et al.* ("Torley I") and U.S. Patent No. 4,876,252 to Torley *et al.* ("Torley II").

Green recites compounds wherein the group corresponding to the variable R_1 of the present claims is furyl, pyrazolyl, triazolyl or isoxazolyl (see Green, column 4, lines 20-27). Amended claim 1 does not recite that R_1 can be furyl, pyrazolyl, triazolyl or isoxazolyl and,

accordingly, is not anticipated by Green. Claims 7 and 11 each depend from claim 1 and, accordingly, are not anticipated by Green.

Davis I and Davis II (a continuation of Davis I) recite compounds wherein the group corresponding to the variable R_1 of the present claims is pyridine (see formula (1) at column 2, lines 1-10 of Davis I and Davis II). Amended claim 1 does not recite that R_1 can be pyridine and, accordingly, is not anticipated by Davis I or Davis II. Claims 7 and 11 each depend from claim 1 and, accordingly, are not anticipated by Davis I or Davis II.

The compounds of the present claims require a phenyl group substituted by $-C(=O)NR^5R^6$. Torley I and Torley II (a division of Torley I) recite compounds wherein the group corresponding to $-C(=O)NR^5R^6$ of the presently claimed compounds is $-C(=O)NH(CH_2)_nNRR$ (*i.e.*, one of R^5 and R^6 is H and the other is $(CH_2)_nNRR$. Claim 1 has been amended to no longer recite that R^5 and R^6 can be $-(CH_2)_aNR_9R_{10}$ and, accordingly, is not anticipated by Torley I or Torley II. Claims 7 and 11 each depend from claim 1 and, accordingly, are not anticipated by Torley I or Torley II.

Claim 38 has been canceled without prejudice.

In view of the above amendments and remarks, Applicant believes the rejection of claims 1, 7, 11 and 38 under 35 U.S.C. § 102(b or e) cannot stand and must be withdrawn.

III. Rejection of Claims 1, 2, 7-14, 24-27 and 38-44 Under 35 U.S.C. § 103(a)

Claims 1, 2, 7-14, 24-27 and 38-44 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Green, Davis I, Davis II, Torley I or Torley II. Applicant respectfully submits that the compounds recited in any of pending claims 1, 2, 7-14, 24-27 or 39-44 are not obvious in view of any of Green, Davis I, Davis II, Torley I or Torley II.

Importantly, none of Green, Davis I, Davis II, Torley I or Torley II recite a compound of any of pending claims 1, 2, 7-14, 24-27 or 39-44. Furthermore, there is no suggestion or motivation found in any of Green, Davis I, Davis II, Torley I or Torley II to modify the compounds recited therein to arrive at the compounds of the present claims. When a new chemical entity is claimed, a *prima facie* case of obviousness requires that the prior art suggest the claimed compounds to a person of ordinary skill in the art. *In re Deuel*, 51 F.3d 1552, 1557 (Fed. Cir. 1995). Furthermore, in addition to such suggestion, a reasonable expectation of success is also required in order to support a *prima facie* case of obviousness. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991).

In addition, the Federal Circuit has expressly required that "there must be adequate support in the prior art for the ... change in structure, in order to complete the PTO's *prima facie* case [of obviousness] and shift the burden of going forward to the applicant." *In re Grabiak*, 769 F.2d 729, 731-732 (Fed. Cir. 1985). In *Grabiak*, the court expressly stated that in the absence of a reference showing or suggesting the change, there is inadequate support for a *prima facie* case of obviousness. *Id.* at 732. Thus, in view of *Grabiak*, for a compound that differs from the prior art by at least one atom to be obvious, the Examiner must provide a secondary reference that teaches the interchangeability of such at least one atom of the claimed compound with the corresponding atom of the prior art.

The presently claimed compounds differ from those of Green, Davis I and Davis II by at least an entire cyclic group at the R_1 position and differ from Torley I and Torley II at least by the groups at the R^5 and R^6 positions. No reference has been provided which teaches the interchangeability of the presently claimed R_1 groups with those of Green, Davis I or Davis II or the presently claimed R^5 and R^6 groups with those of Torley I or Torley II. Without such a reference, the obviousness rejection of pending claims 1, 2, 7-14, 24-27 and 39-44 is unsupported and cannot stand. Thus, Applicant submits that a proper *prima facie* case of obviousness has not been shown. In the absence of a proper *prima facie* case of obviousness, an applicant who complies with the other statutory requirements is entitled to a patent. *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992).

In view of the above amendments and remarks, Applicant believes the rejection of claims 1, 2, 7-14, 24-27 and 38-44 under 35 U.S.C. § 103(a) cannot stand and must be withdrawn.

IV. References CG and DD

Applicant submits herewith a supplemental Form PTO-1449 listing literature reference DD with the date provided. Although the Examiner also refers to literature reference CH, it appears that literature reference CG was intended. The date of literature reference CG was previously supplied by Applicant and considered by Examiner Ford on January 15, 2004. A copy of a Form PTO-1449 form with literature reference CG (with publication date provided) initialed by Examiner Ford is attached hereto.

Applicant respectfully requests that the Examiner review the reference identified as DD on the supplemental Form PTO-1449 submitted herewith, and that it be made of record in the file history of the above-identified application.

V. Conclusion

Applicant respectfully requests that the present remarks be made of record in the file history of the present application. An early allowance of the application is earnestly requested. The Examiner is invited to call the undersigned with any questions concerning the foregoing.

It is believed that no fee is due other than that for the extension of time; however, in the event any other fee is required, please charge the required fee to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

Anthony M. Insogna, Reg. No. 35,203

By: Michael J. Bruner, Reg. No. 47,458

Date February 15, 2005

By: Michael J. Bruner (Reg. No. 47,458)
For: Anthony M. Insogna (Reg. No. 35,203)
JONES DAY
222 East 41st Street
New York, New York 10017
(858) 314-1130

Enclosures